IN THE CLAIMS:

Kindly cancel claims 1-52 without prejudice or disclaimer.

Please add the following new claims to the application.

--53. A process for detecting macrolide antibiotic resistance in microorganisms, comprising the steps of:

a) preparing a sample containing microorganisms,

b) contacting the sample with at least one hybridization probe in situ, wherein said hybridization probe is specific for a nucleic acid sequence in microorganisms which is associated with macrolide antibiotic resistance, under conditions which permit the probe to hybridize specifically, and

c) analyzing the sample by determining the appearance of in situ hybridization between said hybridization probe and nucleic acids in said sample as an indication of antibiotic resistance.

54. The process according to claim 53,wherein the microorganisms are selected from the group consisting of bacterial organisms and protozoa.

55. The process according to claim 53, wherein the nucleic acid sequence which is associated with macrolide antibiotic resistance is a ribosomal nucleic acid sequence.

56. The process according to claim 55, wherein said nucleic acid sequence is a bacterial 23 S ribosomal nucleic acid sequence.

57. The process according to claim 56, wherein said

nucleic acid sequence contains a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2 and SEQ ID NO:3.

58.The process according to claim 57, further comprising a hybridization probe specific for a wild type nucleic acid sequence.

59. The process according to claim 58, wherein said wild type nucleic acid sequence includes the sequence according to SEQ ID NO:4.

60. The process according to claim 56, wherein the nucleic acid sequence encompasses a region corresponding to one or more of the nucleotides 2032, 2057, 2058, 2059, 2503 and 2611 on the E.coli 23S rRNA.

61. The process according to claim 53, wherein said microorganisms are slowly growing pathogens and/or pathogens which are difficult to culture, or cannot be cultured in vitro.

62. The process according to claim 61, wherein said microorganisms are selected from the group consisting of Helicobacter, mycobacteria, Porphyromonas gingivalis, Propionibacterium acnes, Borrelia burgdorferi, mycoplasmas, chlamydias, Tropheryma whippelii, bartonellas, legionellas, nocardias and actinomycetes.

63. The process according to claim 53, wherein said sample is derived from human or animal tissues or body fluids.

64. The process according to claim 53, wherein the microorganisms are not cultured prior to contact with said hybridization probe.

65. The process according to claim 53, wherein the sample is subjected to a procedure for enriching microorganisms.

66. The process according to claim 53, wherein a presumptive medium is added to the sample prior to step a).

67. The process according to claim 66, wherein said presumptive medium contains an indicator substance for typing microorganisms.

68. The process according to claim 53, wherein the sample is fixed.

69. The process according to claim 68, wherein said sample is permeabilized.

70. The process according to claim 53, wherein the hybridization probe is selected from the group consisting of nucleic acids and nucleic acid analogues.

71. The process according to claim 70, wherein said nucleic acid analogues are PNA.

72. The process according to claim 70, wherein said nucleic acids are DNA.

73. The process according to claim 53, wherein the hybridization probe includes a hybridization region having a length of 10 to 30 nucleotides.

74. The process according to claim 73, wherein said hybridization probe has a length of 15 to 20 nucleotides.

75. The process according to claim 74, wherein said hybridization probe has a length of 17 to 18 nucleotides.

76. The process according to claim 53, wherein said hybridization probe is specific for mutations selected from deletions, transversions, transitions and modifications of the wild type sequence.

77. The process according to claim 53, wherein several hybridization probes are used which are specific for different nucleic acid sequences associated with antibiotic resistance.

78. The process according to claim 53, wherein said hybridization probe is selected from the group consisting of ClaR1 (SEQ ID NO: I), ClaR2 (SEQ ID NO:2) and ClaR3 (SEQ ID NO:3) .

79. The process according to claim 53, wherein at least one hybridization probe is specific for a nucleic acid sequence from a wild type of the microorganism.

80. The process according to claim 53, wherein at least one hybridization probe is specific for a species or a genus of said microorganism.

81. The process according to claim 53, wherein said hybridization probe carries a direct label.

82. The process according to claim 53, wherein said hybridization probes are labeled, or can be labeled, with dye groups, fluorescence groups and/or enzyme groups.

83. The process according to claim 53, wherein more than one hybridization probe is used and said probes are labeled or can be labeled differently.

84. The process according to claim 53, wherein the sample is analyzed in step c) by microscopic methods.

85. The process according to claim 53, wherein the analysis in step c) comprises quantitatively determining antibiotic resistance.

86. A reagent kit for determining macrolide antibiotic resistance in microorganisms by in-situ hybridization, comprising:

(a) a medium for preparing the sample, and

(b) at least one hybridization probe which is specific for a nucleic acid sequence in microorganisms which is associated with antibiotic resistance.

87.The reagent kit according to claim 86, further comprising at least one hybridization probe which is specific for a species or genus of microorganisms.

88. The reagent kit according to claim 86, wherein the medium for preparing the sample is a presumptive medium and/or a medium for enriching microorganisms.

89. A reagent kit according to claim 88, wherein the presumptive medium comprises a nutrient solution containing a nitrogen source and other essential components.

90. The reagent kit according to claim 89, wherein said presumptive medium further comprises reducing substances and/or oxygen-repelling additives.

91. The reagent kit according to claim 86, further comprising indicator substances which are dissolved and/or suspended in the presumptive medium.

92. An oligonucleotide having a length of 10 to 30 nucleotides, comprising a sequence according to SEQ ID NO:1, 2, 3 or 4 or a part thereof, wherein said part is at least 10 nucleotides in length.

93. The oligonucleotide according to claim 92, further comprising a labeling group.

94. A reagent kit for typing microorganisms and/or determining antibiotic resistance in microorganisms, comprising:

(a) a medium for preparing the sample, and

(b) a means for typing microorganisms and/or for detecting antibiotic resistance.

95. The reagent kit according to claim 94, wherein the medium for preparing the sample is a presumptive medium and/or a medium for enriching microorganisms.

96. A reagent kit according to claim 95, wherein the presumptive medium comprises a nutrient solution containing a nitrogen source and other essential components.

97. The reagent kit according to claim 96, wherein said presumptive medium further comprises reducing substances and/or oxygen-repelling additives.

98. The reagent kit according to claim 94, further comprising indicator substances which are dissolved and/or suspended in the presumptive medium.

99. The reagent kit according to claim 98, wherein said indicator substances include a urease indicator for detecting Helicobacter species.

100. The reagent kit according to claim 99, wherein said urease indicator can detect H. pylori and/or H. heilmannii.

101. The oligonucleotide according to claim 92, wherein said oligonucleotide has a length of 15 to 20 nucleotides.

102. The oligonucleotide according to claim 92, wherein said oligonucleotide has a length of 17 to 18 nucleotides.--

REMARKS

In the Office Action dated November 7, 2002, claims 1-19, 21, 26-42 and 48-52, in the above-identified U.S. patent application were rejected. Reconsideration of the rejections is respectfully requested in view of the above amendments and the following remarks.

The specification was objected to as missing sequence identifiers. Sequence identifiers have been added at pages 32-33 and page 41 of the application. In view of these amendments applicants request that this objection be withdrawn.

Claims 1-19, 21, 26-42 and 48-50 were rejected under 35 USC §112, first paragraph, as lacking enablement. Claims 1-19, 21, 26-42 and 48-50 have been canceled and new claims added to the application. The new claims clarify that the present invention detects macrolide antibiotic resistance in microorganisms. Mutations in the 23S rRNA lead to antibiotic resistance against a plurality of macrolide antibiotics in several organisms such as